FORMATION AND STRUCTURE OF CASEIN MICELLES IN LACTATING MAMMARY TISSUE

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Milk is an unusually stable colloidal system; the stability of this system is due primarily to the formation of micelles by the major milk proteins, the caseins. Numerous models for the structure of casein micelles have been proposed; these models have been formulated on the basis of *in vitro* studies. Synthetic casein micelles (i.e., those formed by mixing the purified α_{s1}- and κ-caseins with Ca^{2+} in appropriate ratios) are dissimilar to those from freshly-drawn milks in (i) size distribution, (ii) ratio of Ca/P, and (iii) solvation (g. water/g. protein). Evidently, *in vivo* organization of the caseins into the micellar form occurs in a manner which is not identical to the *in vitro* mode of formation.

Current theories regarding synthesis of the individual casein components state that their synthesis is controlled by single genes. Chemical evidence suggests that caseins are not synthesized individually, but are initially formed as a single macromolecule consisting of one κ-casein, two β-caseins, and three α_{s1}-caseins of ~150,000 daltons. The mRNA required for such a synthetic process would be of the order of 1.3×10^6 daltons. Following synthesis of the ribosomes of the endoplasmic reticulum (ER), the newly formed "macro-casein" passes via the ER lumen to the area of the Golgi apparatus where phosphorylation, carbohydration, and other modifications vital to micelle formation occur.

We propose that phosphorylation of the macro-casein takes place in Golgi vacuoles (Fig. 1), after which Ca^{2+} is bound in the form of salt bridges, rendering structural stability to the macro-casein complex. Next, an enzyme specific for the cleavage of an arginine-hydrophobic amino acid sequence clips the macro-casein, yielding an N-terminal arginine residue in the region of the phosphorylated sequence of the casein monomers. It is this partially-hydrolyzed macro-casein unit which, through hydrophobic bonding, forms thread-like structures in the Golgi vacuoles (Fig. 1). Then, as the Golgi vacuoles migrate toward the apical region of the cell, these thread-like structures roll up into the porous, solvated aggregate called the casein micelle. Further organization of casein micelles occurs by the formation of calcium phosphate bridges and other ionic bonds between the charged surface amino acid residues. Finally (Fig. 2), the Golgi vacuoles empty their contents (casein micelles, lactose, whey proteins, etc.) into the alveolar lumen. The membrane of the Golgi vacuoles replenishes that part of the plasma membrane which has been ruptured for release of vacuole contents.

These hypotheses concerning the synthesis of casein and formation of casein micelles offer an explanation for (i) the presence of casein components in constant ratios, (ii) the structural stability of casein micelles, and (iii) their sensitivity to rennin and divalent ions.

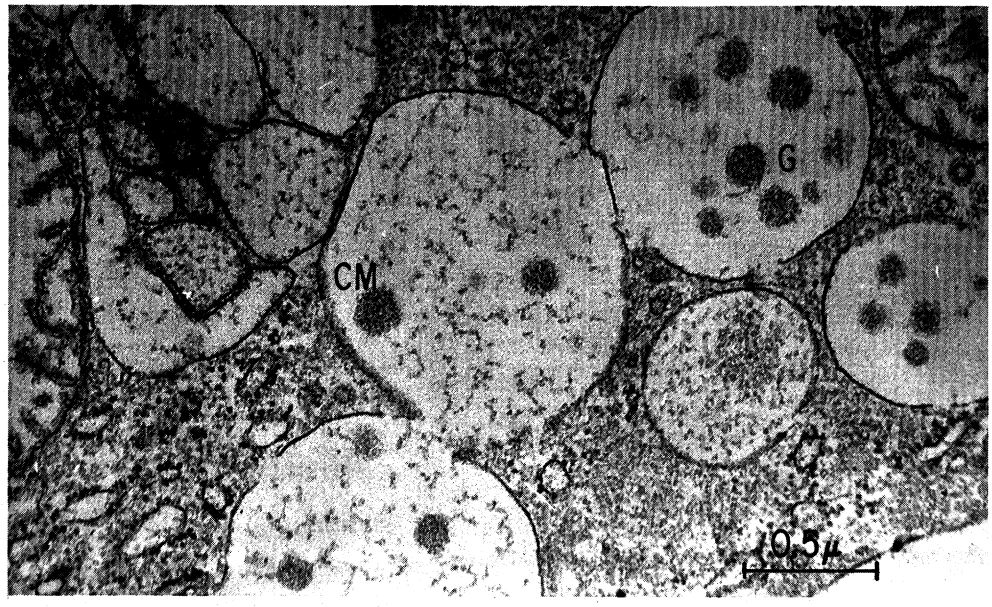

Figure 1. Formation of casein micelles (CM) within Golgi vacuoles (G) of lactating rat mammary gland. Fixed in buffered O_sO_4 - Epon embedded - stained with uranyl acetate and lead citrate.

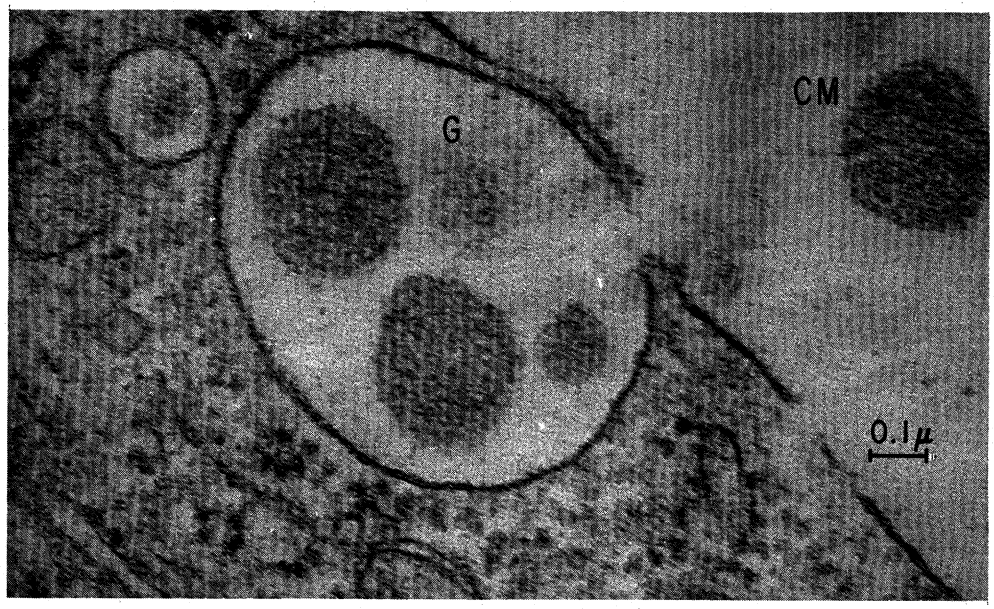

Figure 2. A Golgi vacuole releasing its contents into the alveolar lumen (L).